increased sensitivity of the assay. Moreover, because the extraction is performed in a separate assay chamber, these assays do not require a complex plastic or cardboard housing or specially designed swabs to fit in the complex housings to help control flow of the sample from the sample chamber portion of the housing to the sample receiving region of the immunoassay test strip.

35 U.S.C. § 112

Claims 10-20 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way to reasonably convey to one skilled in the relevant art that the inventor had possession of the claimed invention. Independent Claims 10 and 20 were previously amended to clearly state that the assay chamber provided is separate from the lateral flow immunochromatographic device. Support therefor is found, for example, in Figures 5-7 and at page 43, lines 9-14 of the specification, which depict and describe the placement of the sample receiving region of an immunochromatographic device into contact with the extracted sample after the extraction. One of skill in the art would understand that the non-fluidly connected sample chamber and immunodiagnostic test device shown in Figures 5-7 and described at pages Figures 5-7 and at page 43, lines 9-14 of the specification are "separate" as that term is used in the claimed method. See also Schwartz Decl. (submitted with Preliminary Amendment) at ¶ 4.

Applicants therefor respectfully assert that the amendment does not add new matter, and that the rejection under § 112 should be withdrawn.

E

35 U.S.C. § 102 and 103

Claims 10-11, 13-15, and 17-20 have been rejected as anticipated by Imrich et al. (U.S. Patent No. 5,415,994). Claims 12 and 16 have been rejected under 35 U.S.C. § 103(a) as unpatentable over Imrich et al. in view of Bogart et al. (U.S. Patent No. 5,494, 801) and Murray (U.S. patent No. 3,957,436).

ART BASED REJECTIONS

35 U.S.C. § 102

The Examiner has maintained the rejection of claims 10-11, 13-15 and 17-20 under 35 U.S.C. § 102(b) as anticipated by Imrich et al. (US 5,415,994). 6/27/01 Office Action at ¶ 6. To anticipate a claim, a prior art reference must contain every element of the claim. Motorola Inc. v. Interdigital Technology Corp. 43 USPQ2d (BNA) 1481 (Fed. Cir. 1997).

Independent claims 10 and 20 recite the steps of

(b) "providing an assay chamber which is separate from the lateral flow immunochromatographic device,"

(c) "extracting said antigen from said sample . . . in said assay chamber" and

(d) "inserting said sample receiving region [of the immunochromatographic device device] into said assay chamber and contacting said liquid extract."

The devices in Imrich are described as containing an extraction chamber which is in fluid communication with the immunoassay test strip matrix:

> The devices generally comprise an extraction chamber, a labelling zone having a means for specifically labelling the analyte; and a matrix defining an axial flow path in fluid communication with the extraction chamber, which matrix comprises a sample receiving zone and capture zone located downstream from the sample receiving zone. (col. 2, lines 26-32).

E

Although the examiner suggests that figures 2A and 2B of Imrich et al. illustrate a separate extraction chamber, it is clear from the exemplary description above that the extraction chamber is in fluid communication with the test strip matrix. Although col. 4, lines 4-6 of Imrich do describe a stop means, it further notes that the stop means is "to stop ingress of the sample containing support," that is, to keep the swab from touching the immunoassay test strip. However, at col. 4, lines 24-26, Imrich et al. further states that "[t]he extraction chamber is fluidly connected to the matrix by means of an exit port located distally in the chamber." Thus, although the extraction chamber and matrix are in different regions of the Imrich device, they are fluidly connected. Therefore the methods described in Imrich do not include a step of providing an assay chamber which is physically separate from the lateral flow device.

Moreover, Imrich fails to teach inserting the immunochromatographic test strip into the extracted sample to initiate the assay. In Imrich *et al.* the extraction chamber is in fluid communication with the immunoassay test strip matrix, and the method performed when using the Imrich *et al.* device does not include the step of inserting the sample receiving region of the device into the assay chamber and contacting said liquid extract. Because Imrich fails to disclose those two steps of the claimed method, Imrich cannot anticipate the methods claimed in claims 10 or 20. Nor can Imrich anticipate dependent claims 11, 13--19, or 21 which include the limitations of claim 10 and/or claim 20.

In contrast to the methods described in Imrich, the methods claimed in Claims 10-21 of the instant application are directed to methods in which an assay chamber separate from the immunoassay device is provided in which to perform the sample

extraction. Moreover, in the methods of claims 10-20, the immunoassay device is inserted into the assay chamber to contact the extracted sample after sample extraction, and is not in fluid communication with the assay chamber prior to insertion into the assay chamber.

Applicants therefore respectfully assert that none of the instant claims are anticipated by Imrich et al.

35 U.S.C. § 103

Applicants also respectfully assert that none of the claims are made obvious by Imrich et al. Although the Examiner indicates that Imrich describes the use of separate extraction tubes, it does not appear that Imrich teaches the use of extraction tubes which are not in flow communication with the immunoassay test strip. In addition, Imrich teaches against the use of separate extraction of samples, because separate extraction of samples require the user to "return later to transfer the acid solution to the assay medium. Multi-step assays such as these require more time and attention from health care personnel and thus are more expensive than one step assays." Imrich *et al.* at col. 1, lines 61-66. Imrich also fails to the teach the use of an immunoassay test strip lacking a bulky housing which can be inserted into a separate assay chamber after extraction.

Although the Federal Circuit noted in Interconnect Planning Corp. v. Feil, 227 U.S.P.Q. (BNA) 543 (Fed. Cir. 1985) that the claimed invention and references must each be evaluated as a whole, the Federal Circuit concluded that the district court had improperly reconstructed the claimed invention from separate components in the prior art:

6

> "From its discussion of the prior art it appears to us that the court, guided by the defendants, treated each reference as teaching one or more of the specific components for use in the Feil system, although the Feil system did not then exist. Thus the court reconstructed the Feil system, using the blueprint of the Feil claims. As is well established, this is legal error. Id. at 548.

Moreover, the Federal Circuit further noted that "[t]here must be 'something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination'." Id. at 551 (quoting Lindemann Maschinenfabrik GmbH v. American Hoist and Derrick Co., 730 F2d 1452, 1462, 221 USPQ 481, 488 (Fed. Cir. 1984)). The test that the prior art must be viewed as a whole avoids improper focus on the obviousness of substitutions and differences between the claimed invention and the prior art. Gillette Co. v. S.C. Johnson & Son, 919 F.2d 720, 16 U.S.P.Q.2d (BNA) (Fed. Cir. 1990). Thus, there must be some reason for combining elements other than hindsight reconstruction. Interconnect Planning Corp. at 551. Furthermore, an invention is not unpatentable because it was "obvious to try." In re O'Farrell, 853 F.2d 894, 902, 7 U.S.P.Q. (BNA) 337 (Fed. Cir. 1988).

Here, as discussed above, Imrich describes only the use of devices containing both the immunoassay test strip and an extraction chamber fluidly connected with the test strip. Imrich does not explicitly describe or suggest a method for detecting a Strep A antigen where the assay chamber is separately provided from the immunoassay device and the immunoassay test strip is inserted into the extracted sample to initiate sample flow through the test strip.

In the claimed device, however, spatial separation of the separate assay chamber and lack of fluid communication between the assay chamber and the separate lateral flow immunochromatographic assay test strip permits greater control over the

length and efficiency of extraction, and the sensitivity of the assay. For example, as noted at page 63 of the specification, a device within the scope of the claimed invention is able to detect Streptococcus cells when present at a concentration as low as 4 X 10^5 per swab, while the one-step Quidel device can detect Streptococcus cells only when present at a concentration of 8 X 10^5 cells/swab. In addition, in a study comparing the sensitivity of the OSOM™ Strep A test with the sensitivity of the Quidel QuickVue™ Strep A test, Dr. Richard H. Schwartz determined that the OSOM™ Strep A test had an overall sensitivity of 95%, while the QuickVue™ Strep A test had an overall sensitivity of 87%. Declaration of Richard H. Schwartz at ¶ 3; Schwartz submitted with preliminary amendment, Richard H., Pediatric Infectious Disease J., 16(11):1099-1100 (November 1997), Exhibit 2 to the Declaration of Richard H. Schwartz. The commercial success of the OSOM™ Strep A test also establishes that claim 21, specifying that the assay detects as low as 4 X 10^5 cells/sample, is not obvious in view of Imrich.

The increase in sensitivity observed with the OSOM™ Strep A test is the direct result of providing a separate assay chamber and then inserting the the immunochromatographic device into the assay chamber to initiate lateral flow through the immunochromatographic device, rather than having the extraction chamber in flow communication with the sample receiving region of the immunoassay test strip. Thus, the commercial success of the OSOM product is directly related to the claimed features of the invention which require "providing an assay chamber which his separate from the lateral flow immunochromatographic device," and the need for "inserting said sample receiving region of said lateral flow immunochromatographic device into said assay chamber and contacting said liquid extract" thereby permitting more efficient extraction.

(See Declaration of Richard H. Schwartz at ¶ 4). A finding of non-obviousness is proper where there is evidence of commercial success of a product, having as a critical feature the claimed invention. Perkin-Elmer Corp. v. ComputerVision Corp., 732 F.2d 888, 221 USPQ 669 (Fed. Cir.), cert. denied, 469 U.S. 857)1994.

Moreover, other immunoassays in use prior to these one-step assays required further manipulation of the sample, such as pipetting or pouring, following extraction of the sample. (Declaration of Richard H. Schwartz at ¶ 6). This introduced additional sources of error into the test and required performance of the test by more qualified personnel. (Declaration of Richard H. Schwartz at ¶ 6).

As discussed above, Imrich teaches away from using a separate extraction procedure requiring the user to return later to initiate flow through the immunochromatographic device. See Imrich at col. 1., lines 61-66.

In addition, because other references describe one-step methods using devices with unwieldy plastic housings unlikely to fit within a sample chamber small enough to obtain efficient extraction, it is not obvious in view of that art to provide a separate sample chamber and insert the immunoassay device into the sample chamber to initiate the assay.

Moreover, taken together, Imrich, Bogart, and Murray (US 3,957,436) do not teach a method for determining the presence or absence of a Streptococcus antigen, where separate immunoassay devices and an extraction chamber are provided, where the extraction solution comprises 0.2-5M sodium nitrite and 0.02-2M acetic acid, or where the solution contains a color indicator to indicate proper preparation. As discussed above, Imrich fails to teach or suggest a method for the detection of an

E

analyte where the immunoassay test strip is not in flow communication with the extraction chamber. In addition, as noted at page 10 of the Office action mailed 9/2/98, Imrich does not teach vigorous mixing of the swab and extraction reagents for at least 10 seconds, or an extraction solution where the addition of 0.3 M acetic acid to a color-indicator spiked 2 M sodium nitrite solution changes the color of the final extraction solution.

Applicants therefore respectfully assert that neither claims 12 and 16, nor claims 11, 13-15 or 17-21 are obvious in light of Imrich et al., either alone or in combination with Bogart and/or Murray.

CONCLUSION

For the reasons set forth above, Applicants believe that claims 10-21 clearly state that the claimed invention is directed to a method for detecting a Streptococcus antigen where an immunoassay device, and a separate assay chamber are provided. The claims also clearly state that the immunoassay device is inserted into the assay chamber after completion of extraction of the sample. Moreover, Applicants respectfully assert that the claims are not anticipated nor made obvious by Imrich et al., which describes only methods using devices in which the immunoassay test strip is in flow communication with the extraction chamber. Applicants thus believe that the claims are in condition for allowance.

Respectfully submitted,

Dated: September 27, 2001

By: Vicki G. Norton

Vicki G. Norton
Reg. No. 40,745

Brobeck, Phleger & Harrison LLP
12390 El Camino Real
San Diego, California 92130-2081
Tel. No.: (858) 720-2500
Fax No.: (858) 720-2555

E